57. (amended) The method of claim 38, wherein the expression of the nucleic acid molecule in the sample is determined by determining the hybridization between the agent and the nucleic acid molecule.

58. (amended) The method of claim 57, wherein the hybridization between the agent and the nucleic acid molecule is determined by nucleic acid amplification.

REMARKS

Claims 1-3, 6, 7, 17-19, 38, 53, 57-59 and 61 were previously pending in this application. By this amendment, Claims 1, 38, 53, 57 and 58 have been amended. As a result, claims 1-3, 6, 7, 17-19, 38, 53 and 57-59 are pending for examination. Support for the amendment to claims 1 and 38 comes from the hybridization conditions provided in the specification and examples. Support for the amendments to claims 53, 57 and 58 comes from the description of these aspects of the invention in the specification. No new matter has been added.

Rejection Under 35 U.S.C. § 112, First Paragraph

New matter rejections

The Examiner has rejected claim 7 as containing new matter for its recitation of the number "15" as the lower limit on fragment size. The Examiner stated that the specification does not disclose a fragment of this length. Applicant respectfully disagrees.

As stated in the previous amendment, in which claim 7 was amended, support for the use of "15" can be found in claim 9 as filed, a portion of which is reprinted here for the Examiner's convenience: "...wherein the isolated nucleic acid molecule is at least 15 contiguous nucleotides." Claim 9 depended from claim 7, and thus the phrase "at least 15 contiguous nucleotides" referred to the lower limit of fragment size.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claim 7 under 35 U.S.C. § 112, first paragraph.

Written description rejections

The Examiner has maintained the rejection of claims 1, 7, 17-19, 38 and 53, and rejected claims 57-59 and 61 under 35 U.S.C. § 112, first paragraph as lacking an adequate written description. In particular, the Examiner stated that the specification does not describe the necessary common features or elements of the claimed genus.

The Examiner stated that "unrelated" sequences would hybridize under stringent conditions to SEQ ID NO:4. (Office Action at page 4). According to the Examiner, unrelated sequences are sequences that "are structurally unrelated to SEQ ID NO:8, provided said nucleotide sequence shares a fragment with SEQ ID NO:4." Applicant notes that a sequence that shares enough sequence with SEQ ID NO:4 to hybridize under stringent conditions should by definition be considered a related sequence, not an unrelated sequence.

Applicant demonstrated this notion of related sequences in Example 2 of the specification. In Example 2, Applicant used a PCR-amplified nucleic acid molecule (137 bp) to screen for full-length clones of LAGE-1 gene. 75,000 clones of a cDNA library of LB373-MEL cells were screened using this procedure. Even using reduced stringency conditions (0.4X SSC at 63°C), Applicant found that DNA from only 25 colonies hybridized to the LAGE-1 probe, representing 0.03% of the total number of colonies screened. The same principle was demonstrated in Example 4 for RNA using Northern blot technology. Using high stringency conditions as required by the claims, Applicant asserts that only sequences that are highly related will be identified. Thus, the sequences embraced by the rejected claims represent only related sequences, and not a vast genus of unrelated sequences as alleged by the Examiner.

Regarding claim 7, the Examiner stated that complements of a fragment of SEQ ID NO:4 could be partial complements and thus could share only a few nucleotides with the unique fragment. Applicant asserts that this cannot be, simply from the requirement that the fragment

be at least 15 nucleotides in length – the complement likewise would be at least 15 nucleotides in length.

Moreover, Applicant does not understand how a "complement" can be only partially complementary. Applicant believes that the standard notion of a complement of a nucleic acid molecule is a second antiparallel nucleic acid molecule in which the sequence is complementary so that a double helix can be formed. For every "A" in the first nucleic acid molecule, the complementary second nucleic acid molecule would have a "T", for every "C" in the first nucleic acid molecule, the complementary second nucleic acid molecule would have a "G", and so on.

Applicant therefore respectfully requests reconsideration of the rejection of claim 7 on the basis that it includes the term "complement".

The Examiner's asserted that "there is no structural information of the claimed unique fragments" and that "excluding fragments of SEQ ID NO:8 is not sufficient for the description of the structural properties of the claimed unique fragments." Applicant respectfully requests reconsideration because (1) the structural information is quite clearly provided by the sequence of SEQ ID NO:4 itself, and (2) excluding SEQ ID NO:8 was not intended, nor is it necessary, to provide structural information. Applicant applied the exclusion of SEQ ID NO:8 as a matter of exclusion of known sequences that could otherwise fall within the scope of the claim.

Based on the foregoing, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1, 7, 17-19, 38 and 53 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claim 6 under 35 U.S.C. § 112, first paragraph as lacking an adequate written description. Applicant wishes to clarify for the Examiner the distinction between allelic variants of claim 6 and other variants of SEQ ID NO:4, all of which are included within the scope of claim 1 (provided of course the variants embody the claim elements). Allelic variants are sequences that differ from some reference sequence (i.e., SEQ ID NO:4 in this case) due to natural variations in gene sequences of different individuals in a population. Other variants that would fall within the scope of claim 1 include variants that are made by man, such as using recombinant processes. Thus, the allelic variants are the naturally occurring subset of sequences that differ from SEQ ID NO:4 by a few nucleotides, but are sufficiently similar to hybridize to SEQ ID NO:4 under high stringency conditions.

The Examiner presented other arguments that suggested that there are no limitations on the number of mutational sites of the allelic variants (Office Action at page 6). These arguments completely disregard the limitations of the claimed invention. Applicant is not claiming any possible allelic variant of SEQ ID NO:4. Applicant wishes to claim only those allelic variants that meet the elements of claim 1. Applicant has provided a written description of allelic variants of SEQ ID NO:4, because one of ordinary skill in the art would understand that Applicant provided sufficient information to be in possession of the claimed invention.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claim 6 under 35 U.S.C. § 112, first paragraph.

Enablement rejections

The Examiner has maintained the rejection of claim 38, and rejected claims 57-59 and 61 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. Applicant has amended claim 38 to recite that the method is carried out using agents that hybridize under high stringency hybridization conditions, which conditions are provided in the claim. The rejection as based on the Examiner's arguments related to low stringency conditions and degrees of selectivity is, therefore, obviated.

Further, Applicant notes that the specification contains a description of the use of primer to distinguish between the expression of nucleic acids provided in the instant application. The specification contains a lengthy section on pages 14-15 that teaches one of ordinary skill in the art that certain segments of LAGE and NY-ESO are unique and that primers can be designed that take advantage of the differences in sequence or the differences in size of the amplification product to distinguish between the LAGE and NY-ESO sequences. Thus Applicant has taught one of ordinary skill in the art how to practice the invention throughout the scope of the claims as presently amended.

Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 38, 57-59 and 61 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claim 53 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. Applicant has amended claim 53 to remove the term vaccine from the composition claim. Instead, the claims recites a composition that induces an immune response. Applicant asserts that one of ordinary skill in the art is enabled to make and use the claimed invention as now amended without exercising anything other than routine experimentation. Methods of measuring an immune response are well known in the art, so that the person of skill in the art can readily verify the induction of an immune response using the claimed composition.

Accordingly, Applicant respectfully requests withdrawal of the rejection of claim 53 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claims 1, 38 and 53, and rejected claims 57-59 and 61 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. The Examiner asserted that the claims are not enabled because the protein encoded by the nucleic acid molecules recited in the claims is not predictably translated, i.e., "it is unpredictable whether the encoded LAGE-1 protein exists in nature," and therefore undue experimentation would be required to practice the claimed invention.

Applicant is not certain why the Examiner remains fixated on the translation of protein in rejecting these claims. The rejected independent claims recite nucleic acid molecules (claim 1), methods for diagnosing cancer using the nucleic acid molecules (claim 38) and compositions containing the nucleic acid molecules (claim 53). The claims do not require protein expression or evaluation of protein expression. Accordingly, Applicant respectfully suggests that the Examiner's reliance on protein expression references to show that undue experimentation would be required to practice the invention is misplaced as irrelevant to the claimed invention.

Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 1, 38, 53, 57-59 and 61 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claims 3 and 17-19 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. The basis for the rejection is the alleged unpredictability of the expression of LAGE-1 protein in tumors.

Applicant traverses the rejection and request reconsideration. As for the previous rejection, the claimed invention does not relate to protein expression. Instead, the claimed invention relates to nucleic acid molecules (claim 3), expression vectors containing the nucleic acid molecules (claim 17) and host cells containing the expression vectors (claims 18 and 19). Protein expression, which the Examiner suggests is the source of the lack of enablement of these claims, is not an element of the claims and therefore not a valid basis for rejecting them.

Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 3 and 17-19 under 35 U.S.C. § 112, first paragraph.

Scope rejections

The Examiner has maintained the rejection of claims 1, 7, 17-19, 38 and 53, and rejected claims 57-59 and 61 under 35 U.S.C. § 112, first paragraph, as being overly broad in scope and thus not enabled by the specification. Applicant respectfully traverses the rejection.

The Examiner based this rejection on the notion that the claims include unrelated sequences. Applicant has addressed this notion above in the written description section. Moreover, in view of the amendments to the claims, Applicant asserts that the claims should no longer be considered overly broad in scope.

Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 1, 7, 17-19, 38, 53, 57-59 and 61 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claims 1 and 6 under 35 U.S.C. § 112, first paragraph as being overly broad in scope and thus not enabled by the specification. Applicant respectfully traverses the rejection.

The Examiner based this rejection on the recitation by the Patent Office that the "unpredictability of protein chemistry would apply equally to DNA sequences which encode proteins." (Office Action at page 15). There is no other basis provided for the rejection. Nor is any support provided for the Examiner's position in this respect.

Applicant still believes that this is an irrelevant and insufficient basis for making an enablement rejection of claims that recite nucleic acid molecules. The Examiner has provided no support for the contention that the principles of protein chemistry apply equally to nucleic acid chemistry. Moreover, the Examiner has provided no sound basis for applying the principles of protein chemistry, whatever the unpredictability of those principles may be, to the instant claimed invention.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1 and 6 as not enabled. Should the Examiner continue to maintain this rejection, Applicant respectfully requests an interview with the Examiner and the Examiner's supervisor.

The Examiner has maintained the rejection of claim 38 under 35 U.S.C. § 112, first paragraph as being overly broad in scope and thus not enabled by the specification. Applicant has amended claim 38 and respectfully requests reconsideration of the rejection in view of the amendment. Claim 38 now recites that the method is used for diagnosing cancer.

New enablement rejection

The Examiner has rejected claims 58 and 59 under 35 U.S.C. § 112, first paragraph as being not enabled by the specification. Applicant respectfully traverses the rejection.

The Examiner states that one cannot perform PCR with one primer. It appears that the Examiner has taken the term "an agent" or "the agent" to mean a singular agent.

In patent claim language terms such as "a", "an" and "the" are taken to mean "one or more". This notion is clear from the subject matter of this claims, in which methods such as hybridization and PCR could be used. Hybridization is usually conducted with one probe, while PCR is usually conducted with two or more primers, as noted by the Examiner (although there are many examples in the literature of single primer PCR). In the instant claim, the term "the agent" means one or more agents.

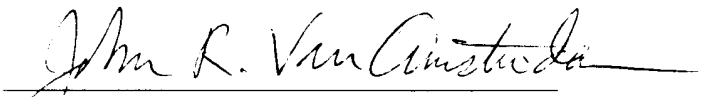
Accordingly, Applicant respectfully requests reconsideration of the rejection of claims 58 and59 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Lethe et al., Applicant



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MARKED-UP CLAIMS

Claims 1, 38, 53, 58 and 59 have been amended as follows:

1. (twice amended) An isolated nucleic acid molecule selected from the group consisting of

(a) a nucleic acid molecule which hybridizes under highly stringent conditions to a molecule having a nucleotide sequence set forth as SEQ ID NO:4, wherein the isolated nucleic acid molecule codes for a LAGE-1 tumor associated polypeptide, and wherein the high stringency hybridization conditions are hybridization at 65°C in hybridization buffer (3.5 x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrolidone, 0.02% Bovine Serum Albumin, 25mM NaH_2PO_4 (pH 7), 0.5% SDS, 2mM EDTA), wherein SSC is 0.15M sodium chloride/0.015M sodium citrate, pH 7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid, or hybridization at 65°C in 3.5X SSC, 1X Denhardt's, 0.5% SDS, EDTA (2 mM), Na_2PO_4 (25 mM) and salmon sperm DNA (100 μg/ml),

(b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and

(c) complete complements of (a) and (b), wherein the isolated nucleic acid molecule excludes nucleic acid molecules having the nucleotide sequence of SEQ ID NO:8.

38. (twice amended) A method for diagnosing cancer [a disorder characterized by expression of a LAGE-1 nucleic acid molecule or an expression product thereof], comprising:

contacting a biological sample isolated from a subject with an agent that [selectively binds] hybridizes under high stringency hybridization conditions to the isolated nucleic acid molecule of claim 1, wherein the high stringency conditions are hybridization at 65°C in hybridization buffer (3.5 x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrolidone, 0.02% Bovine Serum Albumin, 25mM NaH_2PO_4 (pH 7), 0.5% SDS, 2mM EDTA), wherein SSC is 0.15M sodium chloride/0.015M sodium citrate, pH 7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid; or hybridization at 58°C in hybridization buffer containing 10mM TRIS (pH8.8), 50mM KCl and 1.5mM $MgCl_2$, or hybridization at 65°C in 3.5X SSC,

1X Denhardt's, 0.5% SDS, EDTA (2 mM), Na_2PO_4 (25 mM) and salmon sperm DNA (100 µg/ml) and

determining expression of the nucleic acid molecule in the sample, wherein the expression of the nucleic acid molecule is diagnostic for [the disorder] the presence of cancer in the subject.

53. (twice amended) A [vaccine] composition that induces an immune response comprising [a] the nucleic acid of claim 1 encoding LAGE-1 or an immunogenic fragment thereof.

57. (amended) The method of claim 38, wherein the expression of the nucleic acid molecule in the sample is determined by determining the [binding] hybridization between the agent and the nucleic acid molecule.

58. (amended) The method of claim 57, wherein the [binding] hybridization between the agent and the nucleic acid molecule is determined by nucleic acid amplification.